

PATENT COOPERATION TREATY

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JUL 20 2005

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

HAMILTON, BROOK
SMITH & REYNOLDS, P.C.NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

Rec'd IFD

To:

HAMILTON, BROOK, SMITH
& REYNOLDS, P.C.
Attn. Sanders, Deirdre E.
530 Virginia Road
P.O. Box 9133
Concord, MA 01742-9133
UNITED STATES OF AMERICA

(PCT Rule 44.1)

Date of mailing
(day/month/year)

14/07/2005

Applicant's or agent's file reference

3518.1024002

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US2004/039589

International filing date
(day/month/year)

23/11/2004

Applicant

DEPUY SPINE, INC.

FOREIGN DOCKETING

SRW-13AUG2005 WDF-14JUL2005

WOK-14SEP2005

WOM-09OCT2005

Completed By: SSI

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority

European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Eva Boháčová

C178

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 3518.1024002	FOR FURTHER ACTION <div style="text-align: right; font-size: small;">see Form PCT/ISA/220 as well as, where applicable, item 5 below.</div>	
International application No. PCT/US2004/039589	International filing date (day/month/year) 23/11/2004	(Earliest) Priority Date (day/month/year) 26/11/2003
Applicant DEPUY SPINE, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ Certain claims were found unsearchable (See Box II).

3. ☒ Unity of invention is lacking (see Box III).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

National Application No
PCT/US2004/039589

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61P19/10 A61K39/395 A61K45/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 950 417 A (PFIZER PRODUCTS INC) 20 October 1999 (1999-10-20) paragraphs '0031! - '0033!, '0036!, '0037!, '0066!, '0067!, '0113!, '0120! - '0122!; claims 4,10,15 -----	1-5, 7-10,89
X	YAFFE A ET AL: "Combined local application of tetracycline and bisphosphonate reduces alveolar bone resorption in rats" JOURNAL OF PERIODONTOLOGY 01 JUL 2003 UNITED STATES, vol. 74, no. 7, 1 July 2003 (2003-07-01), pages 1038-1042, XP009044957 ISSN: 0022-3492 abstract ----- -/--	1-3

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

11 March 2005

Date of mailing of the international search report

14. 07. 2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Escolar Blasco, P

INTERNATIONAL SEARCH REPORT

national Application No

PCT/US2004/039589

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/207827 A1 (BOYLE WILLIAM J 'US! ET AL) 6 November 2003 (2003-11-06) paragraphs '0087! - '0108! -----	1-10,89
X	WO 99/45923 A (MERCK & CO., INC; FISHER, JOHN, E; RODAN, GIDEON, A) 16 September 1999 (1999-09-16) page 5, lines 24-30 page 20, lines 17-31 -----	1-5, 7-10,89
X	CRANDALL C: "Combination treatment of osteoporosis: A clinical review" JOURNAL OF WOMEN'S HEALTH AND GENDER-BASED MEDICINE 2002 UNITED STATES, vol. 11, no. 3, 2002, pages 211-224, XP009044958 ISSN: 1524-6094 page 216, right-hand column, paragraph 2 - page 220, right-hand column, paragraph 2; table 1 -----	89
X	EZRA A ET AL: "ADMINISTRATION ROUTES AND DELIVERY SYSTEMS OF BISPHOSPHONATES FOR THE TREATMENT OF BONE RESORPTION" ADVANCED DRUG DELIVERY REVIEWS, AMSTERDAM, NL, vol. 42, no. 3, 31 August 2000 (2000-08-31), pages 175-195, XP001056768 ISSN: 0169-409X page 190 -----	1-5,9,10
A	NAKAMURA K ET AL: "Stimulation of endosteal bone formation by local intraosseous application of basic fibroblast growth factor in rats" REVUE DU RHUMATISME (ENGLISH EDITION) 1997 FRANCE, vol. 64, no. 2, 1997, pages 101-105, XP002320926 ISSN: 1169-8446 abstract -----	1-10,89
A	DESANTIS A ET AL: "Current and emerging therapies in osteoporosis" EXPERT OPINION ON PHARMACOTHERAPY 2002 UNITED KINGDOM, vol. 3, no. 7, 2002, pages 835-843, XP009044945 ISSN: 1465-6566 page 841, right-hand column, paragraph 2 -----	1-10,89

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/039589

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: —
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 1-10, 89: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-10, 89

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10, 89

Treatment of uncoupled resorbing bone (including osteoporotic bones) by administration of a bone forming agent and an anti-resorptive agent, wherein at least the former is locally administered into the bone.

2. claims: 11-20, 51-59, 80-88

Kit (for treating osteoporotic bone) comprising: an osteoconductive/bone growth material, an anti-resorptive agent, and means for delivering said agents into the bone

3. claims: 21-30

Method of treating osteoporosis in a patient by local administration of a highly specific cytokine antagonist into an uncoupled resorbing bone

4. claims: 31-49

Osmotic pump implant for providing sustained delivery of agent/s into a bone

5. claim: 50

Device for providing sustained delivery of an anti-resorptive agent into a bone with chamber, exit port and means for expelling the agent

6. claim: 60

Method of treating an osteoporotic patient by inserting a bone growth agent into a vertebral body, removing a portion of the intervertebral disc and inserting a spinal implant into the created disc space

7. claims: 61-69

kit (for treating osteoporosis) with a bone forming agent and a highly specific cytokine antagonist

8. claim: 70

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of treating a non-tumorous uncoupled resorbing bone
by locally administering an anti-resorptive agent into the
bone

9. claims: 71-79

Drug delivery implant for providing sustained release of a
therapeutic agent to a bone comprising a drug pump and a
carrier

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 240.

Continuation of Box 3.

Claim(s) not searched:

Claims 1-10, 89: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/039589

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0950417	A	20-10-1999	BR 9900775 A	28-03-2000
			CA 2262269 A1	23-08-1999
			EP 0950417 A2	20-10-1999
			JP 11315030 A	16-11-1999
			US 6352970 B1	05-03-2002
			US 2002019351 A1	14-02-2002
US 2003207827	A1	06-11-2003	US 6369027 B1	09-04-2002
			US 6613544 B1	02-09-2003
			AU 710587 B2	23-09-1999
			AU 1468697 A	17-07-1997
			BG 63347 B1	31-10-2001
			BG 101813 A	30-09-1998
			CA 2210467 A1	03-07-1997
			CN 1182452 A	20-05-1998
			CZ 9702538 A3	17-03-1999
			DE 19654610 A1	26-06-1997
			EE 9700164 A	16-02-1998
			EP 0784093 A1	16-07-1997
			EP 0870023 A1	14-10-1998
			FR 2742767 A1	27-06-1997
			GB 2312899 A ,B	12-11-1997
			HU 9801122 A2	28-08-1998
			ID 17460 A	08-01-1998
			JP 11503616 T	30-03-1999
			NO 973699 A	21-10-1997
			NZ 326579 A	28-01-1999
			NZ 332915 A	28-07-2000
			PL 321938 A1	05-01-1998
			SK 110797 A3	12-07-1999
			TR 970550 A2	21-07-1997
			TW 221482 B	01-10-2004
			WO 9723614 A1	03-07-1997
			US 6284485 B1	04-09-2001
			US 6288032 B1	11-09-2001
			US 6284728 B1	04-09-2001
			US 6015938 A	18-01-2000
			US 6284740 B1	04-09-2001
			ZA 9610770 A	22-06-1998
WO 9945923	A	16-09-1999	AU 2901199 A	27-09-1999
			CA 2323448 A1	16-09-1999
			EP 1061917 A1	27-12-2000
			JP 2002506030 T	26-02-2002
			WO 9945923 A1	16-09-1999
			US 2001025028 A1	27-09-2001

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/039589

International filing date (day/month/year)
23.11.2004

Priority date (day/month/year)
26.11.2003

International Patent Classification (IPC) or both national classification and IPC
A61P19/10, A61K39/395, A61K45/06

Applicant
DEPUY SPINE, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Escolar Blasco, P

Telephone No. +49 89 2399-7331



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039589

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039589

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-10,89, in respect of IA

because:

- ☒ the said international application, or the said claims Nos. 1-10, 89 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
- ☒ not complied with for the following reasons:
- see separate sheet**
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-10, 89

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-10, 89
Inventive step (IS)	Yes: Claims	
	No: Claims	1-10,89
Industrial applicability (IA)	Yes: Claims	
	No: Claims	see sep. sheet

2. Citations and explanations

see separate sheet

Comments on item III

Claims 1-10 and 89 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Comments on item IV

The International Examining Authority considers that the International Application does not comply with the requirements of unity of invention (Rule 13.1, 13.2 and 13.3 PCT) for the reasons indicated in the 'Invitation to pay additional fees' of the International Search Report (ISR).

At present, the search made covers only the first group of inventions among the nine groups found. Hence, the present opinion refers only to the claims belonging to the first group of inventions, i.e, claims 1-10 and 89.

Comments on item V

1. The documents cited in the International Search Report correspond respectively to D1-D8. Any reference to the documents in the present written opinion relates to the passages given in said report, unless otherwise indicated.

D1: EP-A-0 950 417

D2: YAFFE A ET AL: "Combined local application of tetracycline and bisphosphonate reduces alveolar bone resorption in rats" JOURNAL OF PERIODONTOLOGY 01 JUL 2003 UNITED STATES, vol. 74, no. 7, 1 July 2003, pages 1038-1042

D3: US 2003/207827 A1

D4: WO 99/45923 A

D5: CRANDALL C: "Combination treatment of osteoporosis: A clinical review" JOURNAL OF WOMEN'S HEALTH AND GENDER-BASED MEDICINE 2002 UNITED STATES, vol. 11, no. 3, 2002, pages 211-224

D6: EZRA A ET AL: "ADMINISTRATION ROUTES AND DELIVERY SYSTEMS OF

BISPHOSPHONATES FOR THE TREATMENT OF BONE RESORPTION"
ADVANCED DRUG DELIVERY REVIEWS, AMSTERDAM, NL, vol. 42, no. 3,
31 August 2000, pages 175-195

- D7: NAKAMURA K ET AL: "Stimulation of endosteal bone formation by local intraosseous application of basic fibroblast growth factor in rats" REVUE DU RHUMATISME (ENGLISH EDITION) 1997 FRANCE, vol. 64, no. 2, 1997, pages 101-105
- D8: DESANTIS A ET AL: "Current and emerging therapies in osteoporosis" EXPERT OPINION ON PHARMACOTHERAPY 2002 UNITED KINGDOM, vol. 3, no. 7, 2002, pages 835-843.

2. As explained in the ISR, both the combination of bone-forming and anti-resorptive agents and its use for treating excess of bone resorption were well known in the art at the date of filing (see D1 to D6). Even though the first approaches to these therapeutic combinations had been done with systemic administration, local delivery to the bone had also been widely disclosed (mainly with biodegradable polymers and osteoconductive materials, see specially D1, D3 and D6).
Reference is made to ISR concerning the specific dependent claims anticipated by each document.
3. For the assessment of the present claims 1-10 and 89 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.